

UNITED STATES DISTRICT COURT  
SOUTHERN DISTRICT OF NEW YORK

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TAKEDA CHEMICAL INDUSTRIES, LTD. and :  
TAKEDA PHARMACEUTICALS NORTH AMERICA, :  
INC., : 03 CIV. 8253 (DLC)

Plaintiffs,

-v-

MYLAN LABORATORIES, INC., MYLAN :  
PHARMACEUTICALS, INC., and UDL :  
LABORATORIES, INC., :

Defendants. :

OPINION & ORDER

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TAKEDA CHEMICAL INDUSTRIES, LTD. and :  
TAKEDA PHARMACEUTICALS NORTH AMERICA, :  
INC., :

Plaintiffs,

-v-

ALPHAPHARM PTY. LTD. and GENPHARM, :  
INC., :

Defendants. :

04 CIV. 1966

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Appearances:

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DENISE COTE, District Judge:

On March 10, 2006, judgment was entered following a non-jury trial in favor of plaintiff and patentee Takeda Pharmaceutical Company, Ltd. (formerly Takeda Chemical Industries, Ltd.), and its affiliate Takeda Pharmaceuticals North America, Inc. (collectively, "Takeda") and against two generic drug companies, Alphapharm Pty. Ltd. and Genpharm, Inc. (collectively, "Alphapharm") and Mylan Laboratories, Inc., Mylan Pharmaceuticals, Inc., and UDL Laboratories, Inc. (collectively, "Mylan"), in connection with the latters' challenges brought under the Hatch-Waxman Act to Takeda's U.S. Patent No. 4,687,777 ("777 Patent"), which protects the invention of the chemical compound known as pioglitazone. Takeda Chemical Industries, Ltd. v. Mylan Laboratories, Inc., 417 F. Supp. 2d 341 (S.D.N.Y. 2006) ("Opinion"). Pioglitazone is a highly successful drug used in the treatment of diabetes.

Takeda has now moved for an award of attorneys' fees against

both defendants, arguing that this is an exceptional case. Takeda contends that each of the defendants lacked a good faith basis for its Hatch-Waxman Act Paragraph IV certification and engaged in litigation misconduct. Takeda's motion is granted.<sup>1</sup>

An award of attorneys' fees should not be made without a careful consideration of the litigation as a whole and the parties' arguments. The framework established by Congress for accelerating the approval process for generic versions of established drugs, however, is not an invitation to frivolous, bad faith attacks on patents.

As described in considerable detail below, Takeda has shown by clear and convincing evidence that Alphapharm and Mylan each filed baseless Paragraph IV certifications attacking the validity of the '777 Patent. Alphapharm's certification, which asserted invalidity due to obviousness, was deeply flawed and Alphapharm revised its theory again and again in a futile effort to state a prima facie case of obviousness. Mylan completely abandoned its Paragraph IV theory of invalidity and proceeded to trial on a contorted claim that Takeda had engaged in inequitable conduct before the Patent and Trademark Office ("PTO"). Beyond their

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<sup>1</sup> The Opinion mistakenly described Howard Rosenberg as one of Alphapharm's trial experts. Opinion at 381 n.64. Howard Rosenberg was a fact witness for Alphapharm. Mylan served Michael Rosenberg's expert report, but before trial withdrew its proffer of him as an expert. The Opinion also erred when, in a moment of unintentional literary homage, it identified Alphapharm's expert Brian Wright, a Professor of Economics at the University of California at Berkeley, as Richard Wright. Id. at 345.

baseless certifications, Alphapharm and Mylan each engaged in other litigation misconduct. Their misconduct was exceptional and fully justifies the award of attorneys' fees.

### **Legal Standard**

By operation of law, Alphapharm and Mylan each infringed Takeda's patent by filing an Abbreviated New Drug Application ("ANDA") to make a generic form of pioglitazone before the expiration of Takeda's '777 Patent. 35 U.S.C. § 271(e)(2). An ANDA announces the intention of the filer to produce a bioequivalent form of a drug already approved by the FDA. When filing the ANDA the applicant must make a certification regarding any patent protecting the drug that will be copied. Both Alphapharm and Mylan chose to make a certification pursuant to 21 U.S.C. § 355(j)(2)(A)(vii) ("Paragraph IV"), certifying that the patent protecting pioglitazone was invalid. In making the certification, Alphapharm and Mylan were required to give Takeda notice of the "'factual and legal basis' of invalidity." Yamanouchi Pharm. Co., Ltd. v. Danbury Pharmacal, Inc., 231 F.3d 1339, 1347 (Fed. Cir. 2000) (citing to 21 U.S.C. § 355 (j)(2)(B) (ii)).

An ANDA filer must "display care and regard for the strict standards of the Hatch-Waxman Act when challenging patent validity." Id. Such challenges are only authorized under the Hatch-Waxman Act "in accordance with strict statutory requirements" and require the challenger to state in the

Paragraph IV certification that "in the opinion of the applicant and to the best of his knowledge, that each patent for which the applicant is seeking approval is invalid." Id. (citation omitted). ANDA filers are thus held to a "duty of due care" under the Hatch-Waxman Act. Id.

Among the remedies that are available when a patent is infringed by the filing of an ANDA is an award of attorneys' fees under 35 U.S.C. § 285 ("Section 285"), which allows the award of attorneys' fees to the prevailing party in "exceptional cases." Id. at § 271(e)(4). The determination of whether a case is exceptional is made by looking at the "totality of the circumstances." Yamanouchi, 231 F.3d at 1347 (citation omitted). In order to justify an attorneys' fees award the evidence that the case is exceptional must be "clear and convincing." Interspiro USA, Inc. v. Figgie Intern. Inc., 18 F.3d 927, 933 (Fed. Cir. 1994). If a case is determined to be exceptional, the decision to grant attorneys' fees is not automatic; an award should only be made when it is separately determined that it is warranted. Id.

Litigation misconduct that may support an "exceptional case" finding under Section 285 includes "vexatious or unjustified litigation or frivolous filings." Glaxo Group Ltd. v. Apotex, Inc., 376 F.3d 1339, 1350 (Fed. Cir. 2004). For example, cases that arise from the filing of an ANDA may become exceptional for purposes of Section 285 "if the ANDA filer makes baseless certifications." Yamanouchi, 231 F.3d at 1347; see also Glaxo

Group, 376 F.3d at 1351 (noting that "baseless accusations of invalidity" permit an award of attorneys' fees against ANDA filers). A baseless certification includes the failure "to present even a prima facie case of invalidity in filing [the] paragraph IV certification." Glaxo Group, 376 F.3d at 1350. The Federal Circuit has cautioned, however, that "the mere fact that a company has filed an ANDA application or certification cannot support a finding of willful infringement for purposes of awarding attorney's fees." Id. at 1350-51 (emphasis supplied). Filing a baseless Paragraph IV certification and proceeding to challenge a patent's validity despite glaring weaknesses in the theory of invalidity constitute litigation misconduct. Id. at 1350. Where a non-prevailing party has pursued litigation in good faith, an award of attorneys' fees is only warranted where that party has engaged in misconduct in the litigation. See Brooks Furniture Mfg., Inc. v. Dutailier Intern. Inc., 393 F.3d 1378, 1381 (Fed. Cir. 2005); Forest Labs., Inc. v. Abbott Labs., 339 F.3d 1324, 1328-29 (Fed. Cir. 2003).

Takeda's motion for an award of attorneys' fees from Alphapharm will be addressed first. This ruling presumes familiarity with the Opinion, which contains the findings of fact and conclusions of law following trial and which is incorporated by reference. Nonetheless, various terms, references and findings which are set out in detail in the Opinion are on occasion also briefly described here.

## Discussion

### I. Alphapharm

#### A. Reliance on Advice of Counsel

Before discussing the merits of the motion addressed to Alphapharm, it is necessary to determine whether Alphapharm may oppose this motion by relying on two opinions of counsel that it first produced to Takeda on April 28, 2006, with its opposition to this motion. For several reasons, it may not.

One of the opinions Alphapharm produced is a letter/memorandum dated July 12, 2003, and signed by Allen Kipnes ("Kipnes"), an attorney with the law firm Watov and Kipnes. Frommer Lawrence & Haug LLP ("Frommer"), Alphapharm's outside counsel, retained Kipnes at the request of Generics [UK], an Alphapharm affiliate, to prepare a legal opinion regarding the validity of the '777 Patent. Kipnes reported that he and medicinal chemist Dr. Edward Glamkowski, with whom Kipnes consulted in preparing his opinion, had concluded that Takeda's previous disclosure of the six-methyl compound, which is referred to as compound (b) in the Opinion and here, in both an earlier patent issued to Takeda and in an article in a scientific journal, rendered pioglitazone obvious. The prior art patent discussed by Kipnes is U.S. Patent No. 4,287,200 ("'200 Patent") and the scientific article is T. Sohda et al., Studies on Antidiabetic Agents. II. Synthesis of 5-[4-(1-Methylcyclohexylmethoxy)-benzyl]] thiazolidine-2,4-dione (ADD-

3878) and its Derivatives, Chem. Pharm. Bull., 30:3580-3600 (1982) ("Sohda II"). Kipnes noted that the '200 Patent was a "broad disclosure of the claims compounds" and that Sohda II was a more specific disclosure in which compound (b) was shown to be "among a group that showed potent activity but considerable increases in body weight and fat." Kipnes took the view that based on the two disclosures, the patent examiner "should have rejected the claims of the application on prior art grounds." At trial, Alphapharm argued that the disclosure of compound (b) in these two pieces of prior art rendered pioglitazone obvious. Specifically, it asserted that the prior art identified compound (b) as a "lead" compound whose investigation would have led to the discovery of pioglitazone.

Kipnes also opined that the differences in toxicity to the liver and heart reported in Table 1 of the '777 Patent between pioglitazone and compound (b) were not surprising, and therefore were insufficient to overcome pioglitazone's prima facie obviousness. See Opinion at 360-62 (describing Table 1). Primarily, Kipnes questioned whether the differences between pioglitazone and the other compounds reported in Table 1 were "material" and also suggested that those reported results contradicted statements made in the '200 Patent and Sohda II.

The second opinion Alphapharm recently produced came from Frommer attorney Jeffrey Hovden ("Hovden"). Hovden indicated that, following receipt of the Kipnes opinion, a synthetic organic chemist Dr. Ali Berkin ("Berkin"), employed by Frommer, prepared Alphapharm's Section 355 Statement under Hovden's



supervision. See Opinion at 366-67 (describing Alphapharm's Section 355 Statement).

Alphapharm was required to disclose any reliance it wished to assert in this lawsuit on advice of counsel by July 30, 2004. Because it did not disclose at that time its intent to rely on an advice of counsel defense in opposing an award of attorneys' fees to Takeda, it may not do so now.

Takeda made no secret that it would move for an award of attorneys' fees in this case. Takeda's complaint explicitly sought an award of attorneys' fees based on a finding that this case is exceptional under 35 U.S.C. § 285. On February 11, 2004, Takeda wrote to warn Alphapharm that its Paragraph IV certification, which had been filed just two weeks earlier, on January 29, 2004, appeared to have "serious omissions and errors." As explained at a conference of July 16, 2004, and as reflected in a Scheduling Order of July 20, 2004 ("July 20 Order"), the defendants' motions to bifurcate discovery and postpone their identification of and discovery concerning any advice of counsel defense were denied due to concerns regarding efficiency, expense, and prejudice.<sup>2</sup> Because the defendants had not yet identified with any clarity the issues as to which they might interpose such a defense, they were required to identify the issues on which they intended to assert an advice of counsel defense by July 30. Following such a disclosure, Takeda could

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<sup>2</sup> Alphapharm noted at the July 16 conference that it wished to preserve its right to take an interlocutory appeal from the Order, but filed no such appeal.

demand production of documents withheld because of an assertion of privilege and take appropriate discovery. On July 30, Alphapharm notified Takeda that it would rely on advice of counsel as to the combination use patent issues only.<sup>3</sup>

Alphapharm also forfeited any right to rely on the Kipnes opinion when it did not identify the document on a privilege log or otherwise in response to Takeda's June 2, 2004 request for production of documents. The request included a demand for all documents concerning any opinion or advice of counsel sought or obtained by the defendants concerning the validity of the '777 Patent. Alphapharm has not given any excuse for this omission. Such an omission is wrongful, and provides an independent basis for the suppression of the Kipnes opinion.

Essentially, Alphapharm made a unilateral decision to disregard the July 20 Order and its discovery obligations, and to grant itself a bifurcation of discovery. Alphapharm's conduct is vexatious and constitutes litigation misconduct.

Of course, the very concerns about delay, expense and prejudice which underlay the decision to deny the motions for bifurcation are resurrected by Alphapharm's attempt at this late date to reopen discovery. Even now, Alphapharm has made only the most limited and piecemeal disclosure of its privileged documents. Takeda would not be required to take this limited

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<sup>3</sup> Alphapharm later retracted that notice, and decided not to waive the privilege even as to the combination use patents. The combination use patents are for the use of pioglitazone in combination with other therapies. See Takeda Chem. Indus., Ltd. v. Watson Pharms., Inc., 329 F. Supp. 2d. 394, 398-99 (S.D.N.Y. 2004).

production at face value, but would be entitled to disclosure of all relevant documents and an opportunity to depose witnesses to test the bona fides of this reliance defense.<sup>4</sup>

Alphapharm asserts that the Court's decision in January of this year, on the eve of trial summations, to take separate briefing on the issue of attorneys' fees following a ruling on the merits of the challenges to the '777 Patent was a decision to bifurcate discovery on the attorneys' fees issue. This argument is frivolous.<sup>5</sup> The briefing schedule for the attorneys' fees motion in 2006 did not vacate the July 2004 Order that discovery would not be bifurcated, and Alphapharm has pointed to nothing that was said during the trial that could lead to a good faith belief that discovery would be reopened. Indeed, the motion papers filed by Alphapharm's co-defendant Mylan in opposition to

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<sup>4</sup> For reasons it is unnecessary to describe here, the Kipnes opinion is deeply flawed and Takeda would have been entitled to show that Alphapharm was well aware of that fact. Based on just the Kipnes opinion and Hovden declaration, Takeda asserts that it would have taken at least five additional depositions if the material had been produced as required in 2004.

<sup>5</sup> Alphapharm's similar argument that in July 2004, the Court "carved out the § 285 issues" is entirely specious. At the July 16 conference, the Court noted that the parties had been unclear on which issues they might assert an advice of counsel defense, and therefore ordered them to give notice by July 30 of every issue on which they intended to assert the defense. In giving this ruling, the Court noted that it would need a lot more information to make a judgment about efficiency and duplication of effort issues that would accompany any bifurcation, if the only issue to which the defense was relevant was the issue of attorneys' fees. Because the defendants never indicated that the only relevant issue was their defense to a demand for attorneys' fees, and never presented the additional information necessary to support their bifurcation motion, there was no basis to bifurcate and no bifurcation even as to attorneys' fees.

this motion for an award of attorneys' fees recognizes, as they must, that Mylan cannot rely on any advice of counsel it previously received but did not disclose in 2004.

The Kipnes opinion has, in any event, very little relevance to either prong of Takeda's motion. It was obtained at least nineteen months after Alphapharm made its decision to file its Paragraph IV certification. As reported by Alphapharm, that decision had been made by November 2, 2001, at the latest; it did not obtain the Kipnes opinion until July 2003.

Similarly, Alphapharm is not in a position to rely on any work done by Berkin. Berkin is a synthetic organic chemist, and Alphapharm moved at trial, successfully, to strike the testimony of Takeda expert Dr. James Hendrickson on the ground that a synthetic organic chemist is not qualified to opine on the selection of a lead compound for further pharmacological development. Takeda Chem. Indus. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 83366 (S.D.N.Y. Jan. 11, 2006). As described in the Opinion, demonstrating that it would be obvious to select compound (b) as a lead compound was critical to Alphapharm's argument that the '777 Patent was invalid.<sup>6</sup> See Opinion at 375-80.

In sum, Alphapharm may not interpose an advice of counsel defense on the motion for an award of attorneys' fees. Indeed, its contention that it is entitled to do so is frivolous and

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<sup>6</sup> Alphapharm used the same argument in its effort to exclude testimony from Takeda expert Dr. Samuel Danishefsky. See Opinion at 373. The Court found that he was superbly qualified to opine in the field of medicinal chemistry. Id.

vexatious.

B. Alphapharm's Paragraph IV Certification

Takeda contends that Alphapharm's January 29, 2004 Section 355 Statement was devoid of merit. Even as described in the Opinion, the Statement contained clear errors as well as arguments that Alphapharm abandoned by the time of trial. Opinion at 366-67. Viewed in its totality, Alphapharm's Section 355 Statement is so devoid of merit and so completely fails to establish a prima facie case of invalidity that it must be described as "baseless." When viewed in the context of the totality of this litigation, the filing strongly supports an award of attorneys' fees.

Despite the obvious deficiencies of its Section 355 Statement, Alphapharm points out that its Statement satisfied all of the "technical" requirements of the Hatch-Waxman Act and that it was supported by both an outside opinion of counsel and the work of three medicinal chemists and one synthetic organic chemist, and that it allowed Takeda to investigate Alphapharm's claims fully. Alphapharm misses the point. The question is not whether the Statement complied with the technical requirements of the Hatch-Waxman Act, but whether the Statement breached the duty of due care that is imposed on ANDA filers by the Hatch-Waxman Act and is so devoid of merit as to be baseless.

This prong of Takeda's motion rests principally on four contentions regarding the Statement. They will be addressed in turn.

1. Selection of Compound (b) as a Lead Compound and Motivation To Optimize It Through Modifications

Takeda contends that Alphapharm's Section 355 Statement does not explain why one of ordinary skill in the art would identify a compound, identified in the Opinion as compound (b), from Sohda II (one of the two writings the Statement identified as prior art) as a lead compound worthy of further investigation.<sup>7</sup> This contention requires some background.

Although Alphapharm's trial presentation was characterized by a constantly shifting set of arguments, Opinion at 372 n.37, the heart of its attack on the '777 Patent relied on the single contention that prior art compound (b) was a lead compound warranting further investigation or optimization, and that the application of two, obvious chemical processes (homologation and "walking the ring") to that compound would have led to the discovery of pioglitazone. Id. at 372. Thus, it was incumbent upon Alphapharm to explain in its Statement what in the prior art would have led one skilled in the art to identify compound (b) as a lead compound. For the reasons explained in detail in the Opinion, the evidence at trial showed that one skilled in the art

would certainly not have concluded that compound (b) should be chosen as a lead compound over the many other more obvious or at the very least similarly interesting choices presented by that prior art. Indeed, Sohda II teaches away from compound (b) when it specifically comments on its negative effects on body weight and brown fat.

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<sup>7</sup> Compound (b) from Table 1 of the '777 Patent was compound 58 in Sohda II.

Opinion at 377.

Despite the centrality of compound (b) to Alphapharm's trial strategy, and the herculean efforts that its trial expert made to explain despite all the evidence to the contrary why Sohda II would lead one skilled in the art to identify compound (b) as a lead compound, see id. at 377-78, the Statement did not even make that argument.<sup>8</sup> The Statement focused instead on two other compounds described in Sohda II, which the Statement then misidentified, see id. at 36-67, as described below. As a consequence, Alphapharm's Statement did not grapple with the many impediments evident in Sohda II for choosing compound (b) as a lead compound. In this regard, it is noteworthy that Dr. Howard Rosenberg ("Rosenberg"), the head of Alphapharm's intellectual property department, a medicinal chemist, and an Alphapharm officer who assisted in formulating the Statement, admitted in his deposition that there was "nothing" to recommend compound (b) over several other compounds, and he only chose it as a lead compound "because it was similar to pioglitazone." Id. at 377. This is a stunning admission that Alphapharm worked backwards

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<sup>8</sup> The Statement does not identify compound (b) as a lead compound. It merely observes that compound (b) was one of several compounds related to pioglitazone that were specifically mentioned in the '200 Patent as an example of the patented formula that has shown both low toxicity and efficacy in mice. The Statement then asserts that "the specific disclosure of [compound (b)] as described in the '200 Patent and [Sohda II] render [sic] the claimed compounds of the '777 patent, including pioglitazone, obvious and therefore unpatentable." There is no explanation for why compound (b) would have stood out from all the other compounds not related to pioglitazone or, for that matter, to the other compounds related to pioglitazone.

from pioglitazone's success to identify what it would contend was a "lead" compound, and relied exclusively on hindsight.<sup>9</sup>

Alphapharm contends in opposition to this motion that Rosenberg did not impermissibly rely on hindsight, but explained in his deposition that compound (b) was identified by Alphapharm as a lead compound because the data presented in Sohda II showed that it was one of seven active compounds. It also asserts that Rosenberg only received the Statement in its final form after it had been filed. But, this analysis of the compound's activity did not appear in the Statement either. In any event, this iteration of Alphapharm's argument is also scientifically worthless.

Sohda II identified three compounds, and not compound (b), as having the most favorable performance. As for the seven compounds with the highest efficacy scores, six of the seven, including compound (b), were identified as having problems with either toxicity or side effects. See Opinion at 376. Sohda II simply does not support the selection of compound (b) as a lead compound. Moreover, whether Rosenberg saw the finalized Statement before its filing is quite beside the point since, as he admitted in his deposition, he "formulated" the opinion of

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<sup>9</sup> Even in opposition to this motion, Alphapharm improperly depends on post-hoc reasoning. It contends that it was obvious to identify compound (b) as a lead compound since it is a homolog of a compound covered by the '777 Patent, although not a homolog of pioglitazone. Alphapharm relies on the asserted legal principle that homologs are presumed to be prima facie obvious. This can not explain, however, why compound (b) would have been identified by one skilled in the art as a compound worthy of further investigation.



invalidity on which Alphapharm's Statement was premised.

Alphapharm's Statement is similarly deficient in its explanation of why one skilled in the art would be motivated to modify compound (b) in a way that would lead to the discovery of pioglitazone. In making the argument that one skilled in the art would have learned from Sohda II that an ethyl and methyl are "equivalent with respect to biological activity on a closely related analog of pioglitazone," the Statement misidentified the compounds as having pyridyl rings at their left moiety, while they in fact had benzene rings.<sup>10</sup> Id. at 366-67. While Alphapharm in opposition to this motion asks this Court to find that this error was due to mere sloppiness, in fact the error is more insidious. It underscores that Alphapharm was grasping at straws, and did not act with due care or in good faith.

Alphapharm points out that its expert at trial, Dr. Henry Mosberg ("Mosberg"), referred to these same two misidentified compounds -- compounds 11 and 14 from Sohda II -- as examples of routine methyl-ethyl substitution or homologation.<sup>11</sup> But, there is no discernable pattern of biological activity associated in a comparison of the many compounds listed in Sohda II as having either a methyl or ethyl substituent.<sup>12</sup> Nothing in the prior art

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<sup>10</sup> A benzene ring, in contrast to phenyl ring, does not have a nitrogen atom. Opinion at 382 n.66.

<sup>11</sup> An ethyl group, C<sub>2</sub>H<sub>5</sub>, differs from a methyl, CH<sub>3</sub>, by a single CH<sub>2</sub> group. They are homologs since they differ from each other through the addition of a repeating group, the single CH<sub>2</sub> group.

<sup>12</sup> The term substituent is used in chemistry to describe an atom or group of atoms that is substituted in place of a hydrogen

suggests that substituting an ethyl for a methyl would be of any more assistance in improving a compound's toxicity or efficacy profile than using any of the other many possible substituents or than changing course entirely and adopting a different parent structure. See Opinion at 383. Indeed, a careful reading of Sohda II would lead one skilled in the art to conclude that homologation had no tendency to decrease unwanted side effects. Id. In any event, Alphapharm is mischaracterizing Mosberg's testimony. Mosberg admitted that one of ordinary skill could not use compounds 11 and 14 to predict or extrapolate the effect of homologation to a pyridyl compound. As the trial evidence made abundantly clear, the very best that Mosberg could offer was his opinion that biological activity is unpredictable and it would have been obvious to try homologation. This is a far cry from evidence that one skilled in the art would have had any reasonable basis to expect success from homologation. Id. at 384-85.

The Statement was required at a minimum to outline the basis for choosing compound (b) as a lead compound and for modifying it in the ways proposed by Alphapharm at trial. It did not do so. The Statement was critically deficient as a result of these failures.

## 2. Comparison with Ciglitazone

Takeda asserts that the Statement erred when it asserted (1)

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atom.

that Takeda did not demonstrate that pioglitazone was surprisingly superior to another molecule -- ciglitazone<sup>13</sup> -- and (2) that the '777 Patent disclosed an entirely different activity for ciglitazone than was disclosed in the prior art. Alphapharm's Statement contrasts the toxicity of ciglitazone reported in Table 1 of the '777 Patent, where it is described as toxic, and in the prior art, where it is described as having low toxicity. The Statement then observes:

The Applicant of the '777 patent did not explain the contradiction between its application and its prior art disclosure. The prior art undermined the Applicant's conclusion that the data presented in Table 1 actually showed that pioglitazone had surprising or superior toxicity level.

(Emphasis supplied.) The Statement makes largely the same observation in the context of comparing the efficacy of pioglitazone and ciglitazone as presented in the '777 Patent and in the prior art.

These assertions in Alphapharm's Statement were baseless. Alphapharm's Rosenberg admitted that pioglitazone is "clearly superior" because it is non-toxic. Opinion at 385. It is also undisputed that pioglitazone is far more potent than ciglitazone. Id. at 358. One skilled in the art who read the '777 Patent and the prior art would have concluded that the '777 Patent

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<sup>13</sup> Takeda discovered the first thiazolidinedione ("TZD") compounds in the 1970s. By the 1990s, the introduction of TZD pharmaceuticals had revolutionized the treatment of diabetes by enhancing the muscles' ability to take glucose from the bloodstream. Opinion at 347. Takeda synthesized the TZD ciglitazone in 1978, and worked many years to develop it, until it was abandoned during human clinical trials as toxic. Id. at 349. Thereafter, Takeda searched for a compound that was both more potent than ciglitazone and non-toxic. Id.

demonstrated pioglitazone's superiority over ciglitazone and would not have found any contradiction in the differences in the descriptions of ciglitazone's toxicity when it is compared to different groups of compounds. In brief, ciglitazone had low toxicity when compared to other compounds analyzed at the time of Sohda II but was far more toxic than pioglitazone.

Alphapharm's concedes that it abandoned these arguments at trial, noting that it chose to focus on other concerns with Takeda's data.<sup>14</sup> These arguments from its Section 355 Statement were abandoned because they were unsupportable, not because Alphapharm made a tactical decision regarding which argument should be emphasized at trial.

### 3. Table 1's Evidence of Pioglitazone's Superiority

Takeda asserts that Alphapharm's Statement erred when it represented that Table 1 of the '777 Patent does not show the superiority of pioglitazone. As it had done in its discussion of ciglitazone, the Statement compared earlier statements in the prior art describing certain compounds as non-toxic and briefly analyzed the statistical significance levels reported by Takeda in Table 1 to conclude that the "prior art undermined the

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<sup>14</sup> To the extent that Alphapharm tries to explain its abandonment of these arguments by the time restrictions imposed at trial, that excuse is entirely frivolous. There was no limitation imposed on any party in the presentation of its witnesses' direct testimony and none of Alphapharm's experts pressed this point. Nor did Alphapharm contend at trial that it wished to make this argument but could not because of time restrictions.

conclusion that the data presented in Table 1 of the '777 Patent actually showed that pioglitazone had surprising or superior toxicity levels." The Statement went on to point out that several of the comparison compounds had similar (and in the case of one compound superior) efficacy scores to that reported for pioglitazone in Table 1. The Statement concluded that

The similar, or in fact superior activity of the reference compounds coupled with the lack of support of surprising results in the toxicity tests supports the conclusion that whatever credible differences may have been presented in the '777 patent were insufficient to overcome the prima facie case of obviousness.

Alphapharm has not responded to Takeda's contention that an award of attorneys' fees is appropriate because Alphapharm's statement made a baseless claim that the '777 Patent did not show pioglitazone's superiority. At trial, Alphapharm did not reassert this analysis from its Statement, and for good reason. As already noted above, Alphapharm's Rosenberg admitted that pioglitazone was "clearly superior" to compound (b) because of the latter's toxicity. Takeda is correct that the Statement was seriously deficient in this regard as well.

#### 4. Secondary Indicia of Non-Obviousness

Takeda asserts that the Statement is deficient because it did not address sufficiently the secondary indicia of non-obviousness, such as the commercial success of Actos®, the brand name for the compound containing pioglitazone. Alphapharm responds that it could not address secondary considerations relevant to the issue of obviousness in its Statement since none

of the information relevant to those considerations was in Alphapharm's possession at the time the Statement was drafted and it required discovery of Takeda. In particular, it contends that it could not comment on the substantial commercial success of Actos® without obtaining information about the marketing of the drug, and Takeda's profits and forecasts. The most important fact concerning non-obviousness, the significant commercial success of Actos®, was well known to Alphapharm and required no discovery. The Statement was deficient in this regard as well.

In sum, several of the deficiencies Takeda has identified in Alphapharm's Statement are so glaring that, by themselves, they defeat any assertion that the Statement gave adequate notice of the factual basis of invalidity, was drafted with due care, or presented a prima facie case for invalidity due to obviousness.<sup>15</sup> Considered together they highlight that Alphapharm not only abrogated the duty of due care to which ANDA filers are held but acted in bad faith in filing its Paragraph IV certification.

#### C. Alphapharm's Litigation Misconduct

Takeda also asserts that this is an exceptional case because Alphapharm engaged in litigation misconduct following the filing of its Section 355 Statement. It asserts first that Alphapharm largely abandoned the articulation of obviousness in its Section 355 Statement, and presented an ever-shifting collage of

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<sup>15</sup> This is particularly apparent because, as Alphapharm's Statement acknowledges, it had to prove its case by clear and convincing evidence. See Opinion at 371.

arguments in a futile search for a coherent theory of obviousness. Second, without any reasonable basis and in bad faith, Alphapharm attempted at trial to convert its attack on the '777 Patent into an inequitable conduct claim. Third, as already discussed, in response to this motion, Alphapharm ignored the July 20 Order and offered an untimely advice of counsel defense.

#### 1. Alphapharm's Search for a Theory of Obviousness

Some of the highlights in the evolution of Alphapharm's obviousness argument are as follows. As already described, Alphapharm's Rosenberg used hindsight at his deposition to explain why compound (b) would have been selected as a lead compound. That deposition occurred on March 18 and March 30, 2005. Essentially, Rosenberg identified ten lead compounds that could be identified from the prior art and several categories of substituents that it would be useful to test to compare biological activity.<sup>16</sup> This protocol would have required the testing of hundreds of lead compounds and could not be the basis of a challenge to the '777 Patent based on obviousness.

Barry Spencer ("Spencer") was Alphapharm's 30(b)(6) witness, and testified on May 5 and 6, 2005. He presented a complex roadmap that he asserted would have led one skilled in the art to identify two compounds as lead compounds, compound (b) being one

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<sup>16</sup> Rosenberg identified chlorides, halides and CF<sub>3</sub> as substituents to test, but did not identify ethyls. Pioglitazone has an ethyl substituent at its left moiety, the end of the compound at issue here.

of the two. This was an entirely different analysis than laid out in the Statement or described by Rosenberg, who had contributed to the drafting of the Statement. Using biological activity data from Sohda II, Spencer identified thirty-six compounds of interest, and added a thirty-seventh recommended by the author of Sohda II. Purporting to use information from Sohda II about toxicity and side effects, he narrowed the list to twenty-six. Then, using a 1980 declaration from Takeda employee and co-inventor on the '777 Patent Dr. Takeshi Fujita ("Fujita") filed in connection with an earlier Takeda patent, he narrowed the list to three. Alphapharm's Statement, however, had not identified this declaration as prior art. In any event, Spencer then eliminated one of the three because the data in the prior art indicated that it had a lower efficacy index than ciglitazone.<sup>17</sup>

Within two months of Spencer's deposition, Alphapharm changed course again. On July 15, 2005, it served Mosberg's expert report. Mosberg identified yet new sources of prior art: two other Takeda patents, the '779 and '605 patents, and their file histories. Based on the prior art, Mosberg posited that one skilled in the art would have identified compound (b) as a lead compound. Mosberg asserted that one skilled in the art would also have engaged in two steps to alter compound (b) and create

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<sup>17</sup> Spencer had no response when confronted at his deposition with the passage in Sodha II that warned of negative side effects generated by compound (b). He simply acknowledged the passage but continued to insist that compound (b) would be one of the compounds that would have been selected for further development.



pioglitazone: homologation and then walking the ethylated compound around the pyridyl ring that lies at the left moiety of the compound. A description of these processes can be found in the Opinion at 381-85. Mosberg did not point to anything from the prior art, however, to support a reasonable belief that the homologation and ring walking would improve a compound's efficacy and toxicity profiles. As Mosberg's notes, introduced at trial, showed, all he could assert was that these processes were "obvious to try". Id. at 384. Even at trial, the best that he could offer was that anything can happen when one modifies a compound, so a change for the better would not be surprising. Id. at 385.

Then, at his deposition on September 19 and 20, 2005, Mosberg asserted that one skilled in the art would have investigated all 2-pyridyl, 3-pyridyl, and to a lesser extent 4-pyridyl compounds.<sup>18</sup> Pioglitazone is a 2-pyridyl compound.

At trial, Mosberg again relied on the '779 patent<sup>19</sup> and identified compound (b) as a lead compound. When confronted with the many problems associated with the identification of compound (b) as a lead compound based on the prior art, Mosberg turned the identification of a lead compound on its head. He asserted,

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<sup>18</sup> The number indicates the position at which the pyridyl ring is attached to the body of the molecule, counting from the highest atomic weight atom in the ring and moving counter-clockwise.

<sup>19</sup> Takeda suggests that Mosberg relied on both the '779 and '605 patents at trial, but the '605 patent is not mentioned in his trial declaration. Alphapharm nonetheless repeatedly relied on the '605 patent, identifying it as one of six pieces of prior art in its opening trial memorandum.

without any analytical or scientific support, that one skilled in the art would have selected compound (b) for further investigation because the prior art indicated that Takeda was not actively pursuing it, and Takeda would have had an advantage in the development of those compounds in which it had a head start. Id. at 377.

Alphapharm's response to this damning recitation of its ever-evolving theory of obviousness underscores its bad faith. It excuses Spencer's testimony on the ground that he is not a medicinal chemist and testified before Alphapharm had retained Mosberg. It characterizes the differences between Spencer's analysis and Mosberg's as "slight", when they are enormous. Finally, it justifies at least some of Mosberg's innovations on the ground that they should not have been surprising to Takeda.<sup>20</sup>

As for the iterations of its obviousness claim presented at trial, Alphapharm does not grapple with its utter failure to show why compound (b) would be selected as a lead compound. Instead, it now contends that the identification of a lead compound is simply not a part of the obviousness analysis since (1) pioglitazone is closely related to compound (b), which was disclosed in the prior art, and (2) closely related compounds are presumed to have similar properties and are considered prima facie obvious over the prior art. With this argument, Alphapharm essentially concedes that the many contradictory justifications

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<sup>20</sup> In this connection, Alphapharm refers to evidence provided by Dr. Douglas Morton from The Upjohn Company, Takeda's research partner in the development of pioglitazone.

presented in its Section 355 Statement and by its witnesses for the selection of compound (b) as a lead compound were utterly indefensible and fatally flawed.

Instead of defending the selection of compound (b) as a lead compound whose investigation would have led to the discovery of pioglitazone, Alphapharm asserts simply that the Manual of Patent Examining Procedure ("MPEP") allows a presumption that homologs have similar properties, and then tries to explain why the data presented by Takeda in Table 1 of the '777 Patent -- data which shows the superiority of pioglitazone -- were insufficient to rebut the presumption. See U.S. Patent & Trademark Office, Manual of Patent Examining Procedure, § 2144.09 (8th ed. 2001). To do this, Alphapharm makes an entirely misleading presentation.

Alphapharm's brief in opposition to this motion contains a chart with quotations from three Takeda patents that preceded the '777 Patent. The quotations refer to TZDs<sup>21</sup> as a class and assert that they have low toxicity. The chart presents the statements, however, as if they represent a relative assessment of compound (b)'s toxicity profile. As explained in the Opinion, however, the facts laid out in Table 1 are to the contrary. Compound (b) is quite toxic, a fact that underscores the unexpectedness in the discovery of pioglitazone's nontoxicity. Opinion at 385. Again, Rosenberg admitted in his deposition that pioglitazone is clearly superior to the closest prior art, and that Table 1 of the '777 Patent established that clear

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<sup>21</sup> TZD's are a class of compounds developed by Takeda for treating diabetes. See Opinion at 347. Pioglitazone is a TZD.

superiority. It was improper of Alphapharm to continue to contest that issue after Rosenberg's deposition, and it is doubly wrongful for it to make that misleading argument at this late stage.

In any event, Alphapharm's legal analysis is flat wrong. The law requires Alphapharm to show that the prior art gave a reason or motivation to make the claimed composition. Opinion at 371 (citing Yamanouchi, 231 F.3d at 1343). As an initial matter, one must identify a lead compound that one skilled in the art would be motivated to modify. Alphapharm was never able to defend its identification of compound (b) as a lead compound. Moreover, the MPEP itself cautions against equating homology with prima facie obviousness. MPEP at § 2144.09.

Alphapharm similarly misrepresents Mosberg's testimony about the expectations that one skilled in the art would reasonably have from applying the processes of homologation and ring walking to compound (b). Relying on quotations from Mosberg's expert report and trial declaration,<sup>22</sup> Alphapharm contends in opposition to this motion that Mosberg opined that a skilled artisan would have had a reasonable expectation of successfully obtaining a better drug albeit not necessarily a blockbuster drug. First, no one but Alphapharm has suggested that the relevant test is an expectation of a discovery of a blockbuster drug. Second, Alphapharm has simply ignored Mosberg's many concessions in his

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<sup>22</sup> The trial witnesses presented their direct testimony through affidavits or declarations. Opinion at 344.

writings, and deposition and trial testimony that entirely eviscerate the formulations in his report and declaration. These include his acknowledgment that the biological effects of various substituents are unpredictable and that improvements in efficacy and toxicity profiles from homologation and ring walking were neither expected nor unexpected. Opinion at 384-85 and n.74. By summation, Alphapharm's counsel could do little to cabin the damage done by Mosberg's trial testimony, and argued simply that an improvement in a compound's profile would not be surprising. Id. at 385. That, of course, falls far short of evidence of a reasonable expectation of success.

Alphapharm had over two years between the time it decided to file a Paragraph IV certification and its filing of its Statement. The assertion of obviousness in a Section 355 Statement must be rooted in an analysis of prior art and made with due care. Alphapharm was still searching for a viable theory at trial. It has utterly failed to explain why its Statement was so flawed and why its description of obviousness went through such a dramatic evolution between the filing of the Statement and trial. The evidence of Alphapharm's bad faith is overwhelming.

## 2. Alphapharm's Assertions of Inequitable Conduct

At trial, Alphapharm asserted several arguments of little relevance to its claim of obviousness. They are best understood as assertions that Takeda engaged in inequitable conduct.

Because Alphapharm had not pleaded an inequitable conduct claim,

Alphapharm's attempts to insert these new issues created confusion, wasted valuable court time, and increased the burden of the litigation on the parties.

First, in its proposed findings of fact, Alphapharm contended that Takeda presented unreliable data on toxicity to the PTO in the prosecution of the '777 Patent. It then moved to preclude Takeda's toxicology expert from explaining that Alphapharm's assertion was misleading and false. Alphapharm's assertion that the data on toxicity presented to the PTO by Takeda in the '777 Patent could not be replicated and was unreliable rested on test results that only became available five years after the '777 Patent was issued. Takeda Chem. Indus. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 137374, \*3 (S.D.N.Y. Jan. 11, 2006). This argument was entirely frivolous.

Then, at trial Alphapharm appeared to be fashioning an inequitable conduct argument through a comparison of the toxicity data Takeda provided to the PTO for the '777 Patent, and general statements in a prior Takeda patent application about toxicity levels found in TZDs. The comparison was spurious. Opinion at 379 n.58.

Finally, in summation, Alphapharm added yet another new argument. The argument focused on the requirement that a patent contain a description (also called a specification) of the claimed invention "in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains...to make and use the same." 35 U.S.C. § 112. As Alphapharm has had to concede, however, it did not choose to

challenge the '777 Patent based on the adequacy of the specification and this argument was a red herring. The sole challenge brought by Alphapharm was whether the '777 Patent was obvious over the prior art and on this question its legal argument was not as persuasive as Mosberg's own handwritten notes agreeing with Danishefsky's view that based on the prior art, the impact of even small changes in a chemical compound on biological activity was unpredictable. Opinion at 384.

In sum, Alphapharm's arguments that Takeda engaged in inequitable conduct were entirely frivolous. The arguments cannot be excused as mere comment of the credibility of Takeda's witnesses, an argument that Alphapharm makes in opposition to this motion. What Alphapharm's inequitable conduct arguments underscore is that it had lost all confidence in its claim of obviousness, and was grasping at straws. This conduct further supports the award of attorneys' fees.

#### D. Totality of Circumstances

Alphapharm contends that in deciding whether this is an exceptional case warranting the award of attorneys' fees, the Court should weigh the closeness of the case, the conduct of the parties,<sup>23</sup> and the tactics of all counsel. Weighing these factors does not assist Alphapharm.

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<sup>23</sup> Alphapharm has raised only one claim that Takeda engaged in misconduct in defending the '777 Patent. In a footnote, Alphapharm faults Takeda for raising issues concerning the '902 patent for the first time at trial.

This case was not close. Alphapharm's evidence fell woefully short of demonstrating a credible claim of obviousness. The claim of obviousness was asserted without due care and prosecuted in bad faith. As already demonstrated, Alphapharm's conduct of the litigation and tactics were deeply flawed.

Alphapharm identifies a few specific factors to weigh in its favor. It contends that Mosberg's reliance on the '605 and '779 patents as relevant prior art, references which were not disclosed in its Section 355 Statement, was an appropriate response to Takeda's contention that Sohda II taught away from compound (b) as a lead compound. The fact that Sohda II taught away from compound (b), however, was not news.<sup>24</sup> The Statement did not even identify compound (b) as a compound of interest disclosed in Sohda II. To the extent that the '605 and '779 patents provided any support for the selection of compound (b) as a lead compound, then Alphapharm was under an obligation to identify these two references in its Statement.

Alphapharm contends that it "took steps at every juncture to simplify the issues" for trial, pointing to its consent to the severance of the trial of the claims associated with the combination use patents, its completion of fact discovery during the time allowed, its withdrawal of its jury demand, its reduced

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<sup>24</sup> Sohda II identified three compounds, none of which was compound (b), as exhibiting the most favorable properties in terms of activity and toxicity. It warned that compound (b) caused considerable increases in body weight and brown fat. Opinion at 375-76.



request for time to present its case at trial,<sup>25</sup> and its use of only two experts. Alphapharm has not shown, however, that these decisions were anything other than decisions taken in its own interest and/or decisions as to which it had no viable alternative. In any event, they are insufficient when weighed against the other evidence of misconduct described in this Opinion to prevent an award of attorneys' fees.

Alphapharm also asserts that attorneys' fees should not be awarded because it relied upon a well respected and experienced medicinal chemist, Mosberg. Actually, Alphapharm did not rely on Mosberg's analysis until the time of the trial. Mosberg had no role in the formulation of the Statement or in the presentations made by Rosenberg and Spencer. Mosberg's analysis of obviousness was eviscerated at his deposition and trial. Indeed, in opposing this motion, Alphapharm does not rely on Mosberg's explanation of why compound (b) would have been seen by one skilled in the art as a lead compound, relying instead on Rosenberg's analysis, which was also thoroughly discredited at trial. As for the second prong of Mosberg's testimony, his explanation as to why one skilled in the art would have been motivated to apply homologation and ring walking to compound (b) in order to optimize the molecule, during summation Alphapharm's counsel struggled to limit the damage done by Mosberg's testimony on these issues as well. See Opinion at 385.

In contrast to the defendants, Takeda brought to the trial

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<sup>25</sup> Alphapharm notes that it reduced its request to two days, which the Court further reduced to eight hours.

scientists of extraordinary accomplishment and distinction who took the time they needed to study the issues thoroughly and to develop their analyses. See Opinion at 373 n.39. While Mosberg is certainly a respected and experienced medicinal chemist, for whatever reason he did not devote the care and attention to this assignment that it deserved. As a result, he delivered a series of opinions that were completely undercut by a careful examination of the prior art and the application of sound science. Alphapharm must bear the responsibility for this and cannot avoid the imposition of sanctions by hiding behind Mosberg's resume.

In sum, Takeda is entitled to an award of attorneys' fees from Alphapharm. Alphapharm's Section 355 Statement was deeply flawed, filed in bad faith, and fails to present even a prima facie case of invalidity. Alphapharma made these proceedings far more complex and expensive by constantly shifting its theory of obviousness in a futile effort to locate a coherent argument. Even in response to this motion, it has misrepresented the record in this litigation. This is the exceptional case where an examination of the totality of the circumstances amply justifies, indeed compels, the award of attorneys' fees.

## II. Mylan

Takeda has moved for an award of attorneys' fees against Mylan for filing a Paragraph IV certification in bad faith and for litigation misconduct following the close of fact discovery.

Mylan abandoned in its entirety its claim of obviousness contained in its Section 355 Statement, and then after the close of discovery propounded a frivolous claim of inequitable conduct. These, and the other grounds pressed in Takeda's motion, are detailed below.

A. Mylan's Obviousness Claim

Mylan filed a Paragraph IV certification in bad faith and with no reasonable basis to claim that the '777 Patent was invalid. Its Section 355 Statement was deeply flawed and never defended during discovery. Mylan then engaged in further misconduct, attempting to substitute a new theory of obviousness following the close of fact discovery. The Court rejected Mylan's attempt to alter its theory of obviousness at that late stage. Mylan's misconduct was exceptional and deserves the imposition of sanctions.

Mylan decided to challenge the validity of the '777 Patent without any good faith basis to do so. The relevant facts are as follows. Even though it had not yet obtained an opinion to support a Paragraph IV certification, Mylan stationed a person outside the FDA office on May 27, 2003, over six weeks prior to July 15, the first day it could file an ANDA, intending to have a "line stander" hold its place on a 24/7 basis.<sup>26</sup> Mylan had retained the law firm of Foley Hoag, LLP as of April 2003 to analyze the '777 Patent, but the firm was unable to provide an

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<sup>26</sup> The FDA demanded that Mylan's line-stander leave the premises.

opinion of invalidity by July 15. With July 15 swiftly approaching, on July 11, Mylan hired Levy & Grandinetti, a two person law firm, to prepare an opinion, and the firm did so after just sixteen hours of work. Mylan did not produce that opinion during the course of this litigation. With the opinion in hand, it made its ANDA filing on July 15, and then returned to Foley Hoag, which completed its work in August. Foley Hoag was not responsible for preparing Mylan's Section 355 Statement, however, and its August opinion was not produced in this litigation either. Instead, Mylan retained its trial counsel, Cohen, Pontani, Lieberman & Pavane, to prepare its Statement, which was filed on September 8, 2003. Within five weeks, on October 13, Takeda warned Mylan that its certification lacked merit and was an abuse of the statute and the rules.

Mylan's Section 355 Statement identified two pieces of prior art, the '200 Patent and Sohda II. It argued that one compound with a benzene ring at its left moiety made the invention of pioglitazone obvious. (The pioglitazone molecule had a pyridyl ring, not a benzene ring, at its left-moiety.) Mylan misdescribed the benzene compound's structural relationship to pioglitazone and its efficacy as disclosed in Sohda II. Opinion at 367-68. It also gave no reason to select the compound as a lead compound warranting further investigation and optimization.

Mylan resisted discovery of its theory of obviousness, and then when again ordered by the Court after the close of fact discovery to do so, it gave notice that it had abandoned the theory of obviousness set forth in the Statement. See Takeda

Chem. Indus. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2005 WL 2092920, \*1 (S.D.N.Y. Aug. 31, 2005); Takeda Chem. Indus. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC) (S.D.N.Y. entered on June 21, 2005) (Memorandum Opinion and Order limiting Mylan's presentation of evidence at trial to theories set forth in September 8, 2003 Notice). In its stead, Mylan sought to substitute a new theory of obviousness based on a different compound mentioned in Sohda II. The Mylan Statement had focused on compound 14; Mylan's new theory focused on compound 57 (which was described at trial as compound 3894, a compound that had an unsubstituted pyridyl ring as its left moiety). Mylan did not give any detailed explanation of why compound 57 would have been identified by one skilled in the art as a lead compound, or how its optimization would have led to the discovery of pioglitazone. This theory was also advanced in bad faith: Mylan's 30(b)(6) witness had just days earlier indicated that an analysis of the toxicity and efficacy profile of compound 57 would have ruled it out as a lead compound.

In an Order entered on June 21, 2005, Takeda's motion to preclude Mylan from asserting this revised theory of obviousness was granted. Mylan then moved for reconsideration, inappropriately raising several new arguments and making legal arguments that were absolutely frivolous. Takeda Chem. Indus. v. Mylan Labs., Inc., 2005 WL 2092920, \*4. The motion for reconsideration was denied on August 31, 2005. Id. at \*6.

Mylan's defense to this prong of the motion for sanctions is

entirely unpersuasive. Mylan asserts that it did not need a good faith basis to have a line-stander, and argues that Takeda is drawing an impermissible negative inference regarding the advice Mylan received from counsel even though Mylan has elected to rely on its right to withhold the opinions as privileged. See Knorr-Bremse Systeme Fuer Nutzfahrzeuge GmbH v. Dana Corp., 383 F.3d 1337, 1344-45 (Fed. Cir. 2004) (en banc).

Mylan also asserts that it is not required to obtain advice from outside counsel so long as it has another basis for a bona fide belief that the '777 Patent was invalid. Mylan asserts that it relied on its in-house patent attorney Shelly Monteleone, who customarily consults with both outside counsel and Mylan scientists before deciding whether an ANDA could be filed. The problem with its assertion of reliance on Monteleone, however, is that she testified that she had no recollection of actually doing any work on the pioglitazone project and could only testify as to her customary practices.

An adverse inference may not be drawn against Mylan for its failure to present an opinion from counsel that could establish its bona fides in filing an ANDA and then its Statement. Without relying on any such inference, however, Takeda has carried its burden of showing that Mylan did not act with due care or in good faith.

As for the substance of its Section 355 Statement, Mylan asserts that it should not be judged against the standard of success at trial, that is, whether it had clear and convincing evidence of obviousness, but rather whether it had "a reasonable

basis" for asserting that one skilled in the art "would be interested in compound 14." Mylan relies on its characterization of compound 14 and pioglitazone as "non-classical bioisosteres", and a purported presumption that compounds that are so related have broadly similar biological properties, automatically rendering pioglitazone obvious in Mylan's view. Mylan points out that, in any event, it dropped the claim, and the mere fact that it had pleaded it does not constitute vexatious litigation.

This defense of the merits of its Section 355 Statement is utterly frivolous, and is further evidence that an award of attorneys' fees against Mylan is appropriate. Sohda II described 101 specific TZD compounds, giving data on each compound's efficacy. Opinion at 350-53. Mylan has never presented any explanation for why one skilled in the art would single out compound 14 in Sohda II as a lead compound warranting further investigation. Mylan's 30(b)(6) witness could not identify any basis to differentiate the compound from the many others that the article described as performing better or as well as it did. Moreover, Mylan has never presented any expert testimony to support its theory that the compound is a bioisostere of pioglitazone. In contrast, Takeda's distinguished expert explained in his expert report that it is not. In any event, neither Mylan's Section 355 Statement, nor its opposition to this motion, present any explanation of why one skilled in the art would have been motivated to make the substantial modifications to compound 14, which has a benzene moiety, to arrive at pioglitazone, which has a pyridyl moiety at its left end.

Finally, Mylan attributes its delay in identifying its second theory of obviousness on Takeda's delay in producing an unredacted version of internal Takeda report A-15-34. See Opinion at 357-58. According to Mylan, the document disclosed that compound 57 (a/k/a compound 3894) had comparable activity and "only slightly greater toxicity" than pioglitazone. It points out that Takeda was not burdened by Mylan's assertion of this revised theory of obviousness since the Court precluded Mylan from asserting it at trial. Mylan contends that its motion for reconsideration was justified since the Court had overlooked the issue of prejudice as articulated in ATD Corp. v. Lydall, Inc., 159 F.3d 534 (Fed. Cir. 1998). As was explained in the decision denying Mylan's motion for reconsideration, Lydall does not require a finding that Takeda had been prejudiced to preclude Mylan's last-ditch obviousness theory, but even if it were necessary to find prejudice, there was ample evidence that Takeda had been prejudiced. Takeda Chem. Indus. v. Mylan Labs., Inc., 2005 WL 2092920, \*5-6.

Mylan's defense of its aborted effort to make a wholesale revision to its obviousness theory is utterly frivolous. As this Court has previously had occasion to point out to Mylan, Takeda Chem. Indus. v. Mylan Labs., Inc., 2005 WL 2092920, at \*4, since an attack based on obviousness must rely on disclosures made in prior art, the existence or receipt of Takeda's internal documents is irrelevant. Either the invention of pioglitazone was obvious based on prior art, or it was not. It is also extremely misleading of Mylan to characterize compound 3894 as



having only slightly greater toxicity than pioglitazone. Compound 3894 was disqualified by Takeda and Upjohn from further consideration in the Fall of 1984 because of its toxicity to the heart. Opinion at 397. Toxicity was of paramount concern to the two companies as they selected the handful of compounds into which they would be investing considerable resources. Id. at 358-59. In contrast to compound 3894, pioglitazone met the companies' toxicity criteria. Id. at 359.

In sum, Mylan's ANDA filing and Statement were baseless and filed in bad faith. On this ground alone, Takeda would be entitled to an award of attorneys' fees.

#### B. Mylan's Litigation Misconduct Associated with Pursuit of an Inequitable Conduct Claim

Takeda also moves for an award of attorneys' fees on the grounds that Mylan (1) did not have a good faith basis for its inequitable misconduct claim; (2) wrongfully delayed disclosing the claim in order to prejudice Takeda; (3) was unable to identify any material misstatement in Takeda's application for the '777 Patent; (4) relied on Dr. Lawrence Hendry ("Hendry") as an expert for issues on which he was not qualified to opine, see Takeda Chem. Indus. v. Mylan Labs., Inc., 03 Civ. 8253 (DLC), 2006 WL 44053 (S.D.N.Y. Jan. 9, 2006)(granting in part Takeda's motion in limine); (5) frivolously asserted that Takeda had suppressed evidence that pioglitazone was toxic to the liver; (6) asserted that compound 3894 was the closest prior art when it knew it was not; and (7) lacked any theory or evidence of

Takeda's intent to mislead the PTO. Mylan responds to only some of these issues. It presents no defense directed specifically to items 4, 5 and 6.

Before analyzing these issues, a brief description of Mylan's claim of inequitable conduct is in order. Mylan's theory of inequitable conduct was cobbled together from arguments addressed principally to two compounds, one of whose test results were reported by Takeda on Table 1 of the '777 Patent, and one whose results were not. Opinion at 390. Mylan argued that Takeda misrepresented the data regarding compound (c)'s potency in order to make it appear that the compound was weaker than pioglitazone. There were a host of problems with this theory, including the fact that Takeda had evidence that compound (c) had failed the chick lens assay test and had therefore been categorically eliminated as a candidate for development because of its toxicity. Id. at n.82. Therefore, whatever its efficacy, pioglitazone could easily be shown as superior to compound (c). With respect to compound 3894, whose test results Takeda did not present to the PTO, Mylan argued that it was the closest prior art to pioglitazone, and that Takeda had a duty to disclose its performance in tests to the PTO. This theory was also fatally flawed for many separate reasons, including the fact that compound 3894 was not the closest prior art, that Takeda had no duty to present the PTO with information about the compound, and that in any event it had been rejected for development by Takeda due to its toxicity to the heart.

Proof of wrongful intent is of course a necessary component

of an inequitable conduct claim. Purdue Pharma L.P. v. Endo Pharms. Inc., 438 F.3d 1123, 1128 (Fed. Cir. 2006); Opinion at 387-88. Mylan never had any evidence of wrongful intent by Takeda, and despite promises at trial that it would produce some, utterly failed to do so. In contrast, there was powerful, irrefutable evidence that Takeda acted with complete integrity in its dealings with the PTO. Opinion at 389-90, 398-99. Among other things, when it made its application to the PTO it presented the very test results upon which it and Upjohn had relied internally in making their joint selection of the compounds into which they would invest further research resources to try to develop a pharmaceutical. Id. at 389, 398.

As for Mylan's delay in asserting this claim, Mylan waited until the end of the period for fact discovery to request leave to amend its answer and counterclaims to assert invalidity based on inequitable conduct. Despite Mylan's tactical maneuvers, designed to hamstring Takeda's ability to confront this new theory, the Court granted Mylan's request. The Court explained that it was doing so because of the public interest in having issues decided on the merits, and not based on a finding either that Mylan had acted with sufficient diligence or that it had a good faith basis for its claim.

Mylan argues that the Court must have found "good cause" for Mylan's amendment of its pleadings to add the inequitable conduct claim since the Court applied that Rule 16, Fed. R. Civ. P., standard when granting the motion to amend. Mylan asserts that it was delayed in bringing its claim of inequitable conduct by

Takeda's failure to complete document production until February 4, 2005, and Mylan's need to translate Japanese documents. It points out that its claim rested in large part on the assertion that back-up for test results listed in Takeda's internal reports and presented to the PTO could not be located in Takeda laboratory notebooks. See Opinion at 390. Mylan asserts that it notified the Court and Takeda through a letter of March 15, 2005, that Takeda may have procured its patent through inequitable conduct.

Mylan further contends that its assertion of inequitable conduct based on compound 3894 was not frivolous because Takeda did not advise the PTO that both pioglitazone and compound 3894 were both five times more potent than ciglitazone despite internal reports indicating that to be true. Further, it argues that since the data indicated that compound 3894's heart toxicity was "at the lowest level used by Takeda to indicate toxicity," the materiality of the omission of a discussion of the compound in the application for the patent was a "close question." Mylan points out that the Opinion containing the judgment of this Court following trial discussed these issues over the course of several pages, which must indicate that the issues were "worthy of serious consideration."

As the Court explained to the parties at the time, its decision to allow Mylan to bring its claim of inequitable conduct was absolutely not a finding that it was timely or meritorious. Nor can the February production of documents justify the assertion of the claim, since the claim was always frivolous.

Mylan's assertions about compound 3894 were particularly egregious, and its continued defense of that assertion in this motion practice is inexcusable. Mylan's expert Hendry admitted at trial that compound 3894 was not the closest prior art to pioglitazone, and by the time of summations Mylan had abandoned any claim that it was. Opinion at 397 n.104. At trial, Mylan scrambled to try to avoid the evidence that the compound was cardio-toxic by, for example, suggesting that further testing and further statistical analysis of the test results were necessary to confirm the toxicity. Mylan did neither, however. Takeda did the additional statistical analysis and reconfirmed the reliability of the finding. Id. at 397-98 and nn.103 & 104.

Mylan does not and cannot point to any passage in the Opinion of February 21, 2006 that suggests that any of its arguments were meritorious. While Takeda conceded that it had made two errors in describing the protocol for its testing to the PTO, neither of those errors was material, neither would have come close to supporting a finding of inequitable conduct, and Mylan does not suggest anything to the contrary in opposing this motion. The Opinion's length was driven in large part by the defendants' presentation of so many different arguments and iterations of those arguments. To place the findings of fact in context it was necessary to explain the history of the discovery of pioglitazone and the science relevant to the many issues raised by the defendants' claims. The length of neither that Opinion nor this can be fairly read as evidence that the defendants' claims had any merit. They did not.

Mylan contends that it had reason to question Fujita's credibility since Takeda was unable to produce laboratory notebooks to confirm all of the experimental data reported in Takeda's internal reports. As was noted above, Fujita led the research effort that resulted in the discovery of the pioglitazone molecule and was named as co-inventor on the '777 Patent. Fujita, who had been long retired from Takeda by the time of this litigation, did not undertake the search for the notebooks during the discovery period and opined that the contemporaneous internal Takeda reports that he authored were reliable and that if notebooks could not be found for some of the results, then some of the notebooks must be missing. See Opinion at 390. There is absolutely no basis to argue, much less find, that Fujita was ever anything but honest.

Mylan asserts that Takeda's motive to mislead the PTO can be found in the admission by an Upjohn witness that patentability was something you are always concerned about, and Mylan's speculation that Takeda did not want to disclose compound 3894 to the PTO because it was well-known in the prior art and not patentable, and yet "comparable to pioglitazone in activity and toxicity." Mylan was not even aware of the existence of this Upjohn witness at the time it moved to amend and plead its inequitable conduct claim. In any event, the Upjohn witness testified at trial that patentability was not a driving consideration since Takeda and Upjohn were focused first and foremost on identifying a compound that was effective with extremely low toxicity. As just explained, Mylan's assertion

that compound 3894 was comparable to pioglitazone is absolutely false and misleading. It could not establish that proposition at trial, and the repetition of the assertion in this motion practice further warrants the award of sanctions.

Takeda has shown that in each of the seven ways it has identified Mylan acted without a reasonable basis and in bad faith in pursuit of its inequitable conduct claim. For these reasons, Takeda is entitled to attorneys' fees for the period following the close of fact discovery.

#### C. Mylan's Other Litigation Misconduct

Takeda also moves for sanctions because other misconduct by Mylan increased the expense and burden of the litigation. It asserts that Mylan (1) disobeyed court orders setting the schedule for depositions and requiring Mylan to produce a 30(b)(6) witness to respond fully to a deposition notice; (2) on the eve of trial tried to revisit earlier discovery rulings; (3) improperly tried to supplement its inequitable conduct theory on the eve of trial and prevent Takeda from responding to the attempt; (4) made an untimely motion for reconsideration regarding a ruling on a motion in limine concerning Hendry, then purported to withdraw it, only to reverse course again in an attempt to reassert the motion.

Mylan does not address the first issue. It asserts that Takeda suffered no prejudice from Mylan's eve of trial efforts, as set out in items 2 and 3, since the Court rebuffed them. As to the fourth item, it asserts that it fully withdrew the motion

for reconsideration, and Takeda was never burdened with the necessity of responding to it in writing.

By themselves, these actions would not support a finding that this is an exceptional case that warrants an award of attorneys' fees. When taken together with the remainder of Mylan's misconduct, however, Takeda has shown that in each instance these actions constitute litigation misconduct and supply additional support for the award.

#### D. Mylan's Remaining Arguments in Opposition

None of Mylan's arguments in opposition to this motion are persuasive or alter the conclusion that the totality of Mylan's conduct in this litigation justifies an award of attorneys' fees. Mylan's opposition to this motion rests principally on policy arguments. It contends that Congress intended to foster ANDA patent litigation when it enacted the Hatch Waxman Act, that twenty-two of the thirty ANDA litigations that yielded a court decision have been decided in favor of the ANDA applicants, and that in nine of those cases the patent was ruled invalid.

There is no basis to find that this award of fees will deter ANDA filings and litigation. This award addresses baseless ANDA filings and the pursuit of frivolous ANDA litigation in bad faith and other litigation misconduct. The Hatch-Waxman Act cannot be read to immunize such conduct.

Mylan also requests a stay of a decision on this motion pending a ruling by the Federal Circuit on the appeal from the judgment entered at the conclusion of the trial and/or the



completion of the litigation on the combination use patents. Mylan's previous request for a stay was denied, and will not be reconsidered here.

Mylan contends that a decision on the motion should not be made because the Court needs to weigh the amount of attorneys' fees being sought, and Takeda has not yet presented a request for a specific award. The amount of any award will be decided after Takeda has submitted its request for a specific amount and the parties are given a full opportunity to be heard as to the size of any award.

Mylan asserts that Takeda's motion should be denied because Takeda (1) moved for an award of attorneys' fees against Mylan in its pre-trial memorandum of law dated November 18, 2005 on the ground that Mylan had filed a baseless Paragraph IV certification, when Glaxo, 376 F.3d at 1351, bars an award when the filing is the sole basis for the motion; and (2) served a bill of costs on April 11, 2006, although a notice of appeal had already been filed and costs cannot be taxed during the pendency of an appeal. As for Takeda's November 18 motion, it did not seek sanctions based on the filing of the certification, but on the grounds both that the certification was baseless and that Mylan had committed "myriad acts of litigation misconduct." Takeda did not catalogue the misconduct in its pretrial memorandum, but has done so now. As for the bill of costs, Takeda explains that it filed it within the time required by the local rule.

Mylan argues that no fees that Takeda incurred before June

6, 2005 should be awarded against it since that is the first date of misconduct alleged by Takeda against Mylan. June 6 is the date Mylan served its supplemental interrogatory responses and asserted for the first time that the '777 Patent was invalid for obviousness on the basis of the prior disclosure of compound 3894. Because Mylan had filed its certification in bad faith, and thereafter participated in the litigation over the validity of the '777 Patent on a frivolous claim of obviousness, it was in a position to move to amend its pleading and assert the claim of inequitable conduct. These actions were inextricably intertwined, and the application to limit the award to the period following June 6, 2005 is denied.

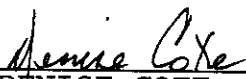
Alphapharm and Mylan point to the remarks of the Court at the conclusion of the trial in which the Court thanked the parties for their hard work and level of preparation. The comments accurately reflect the hard work that each party put into the actual presentation of the evidence during trial, but said nothing about the merits of the parties' legal positions. Those positions were described in the Opinion and here. For the reasons set forth herein, Mylan's case is exceptional and an award of attorneys' fees against Mylan as well as Alphapharm is entirely justified.

**Conclusion**

Takeda's motions for an award of attorneys' fees is granted as to both Mylan and Alphapharm.

SO ORDERED:

Dated: New York, New York  
September 20, 2006

  
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DENISE COTE  
United States District Judge